REMARKS/ARGUMENTS

Claims 41, 42, 59 and 60 stand rejected by the Examiner as allegedly indefinite under 35 U.S.C. §112, second paragraph. The claims have been amended. It is believed that no new matter is added. As amended, it is believed that the claims particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Claims 1-3, 5-8, 12-15, 17-37, 39-41, 43-46, 49-51, 55, 57-59 and 63 stand rejected under 35 U.S.C. §103(a) as allegedly being obvious over Stern et al. (U.S. Patent No. 6,086,918) in view of Habener (U.S. Patent No. 5,120,712), Mandic (U.S. Patent Application Publication No. 2003/0104981) or Barbier et al. (U.S. Patent 6,110,892). This rejection is respectfully traversed. Applicants have amended claim 1 to more clearly define the invention. Support for the amendments may be derived *inter alia* from claim 7 as originally filed; page21, lines 9-13; and page 23 lines 18-20. The present claims all require the selective use of C-terminal amidation in peptides for oral delivery. It is also required that these not be naturally occurring amidated peptides. Hence, amidation is utilized for Applicants' express purpose of enhancing the oral bioavailablity of peptides. Table 8 (page 57) illustrates the significantly enhanced bioavailability that C-terminal amidation imparts to a truncate of parathyroid hormone relative to its free acid analog.

It is urged that one of skill in the art would not be motivated by the teachings of Habener, Mandic or Barbier to selectively choose amidated peptides to the exclusion of other peptides taught by Habener, Mandic or Barbier for insertion into the oral delivery system of Stern. The Examiner cites Habener at column 4, lines 14-25 and at claims 1 and 4 in connection with amidation. However, Habener clearly permits the C-terminus of its peptides to include a wide variety of other functional groups. For example, Column 4, line 20 suggests C-terminal -OH or -OM would be equally useful. Likewise, Mandic does not discuss the enhancement of oral bioavailability and modifies its peptides in at least one of several different ways. See, for example, Mandic at paragraphs 53-57. As noted in paragraphs 59-61 of Mandic, numerous modifications are set forth in the peptides of Figs. 1 and 2 (cited by the Examiner) from which it will not be possible to determine which of the several modifications result in the desired function. Furthermore, given that the function sought by Mandic is not improved oral bioavailability, there is no reason to conclude from Mandic that C-terminal amidation would

enhance oral bioavailability. Likewise, Barbier teaches both amidated and free acid peptides (see Tables 1 and 2) and does not teach that an amidated version would be preferable to a free acid.

Thus, it is urged that none of the secondary references disclose or suggest the selective use of C-terminal amidated peptides in the oral delivery system of the primary reference, Stern. *Prima facie* obviousness is not established where, as here, the cited prior art does not motivate one of skill in the art to select Applicants' compounds to the exclusion of several alternative molecular structures for further combination with the other references. See *Takeda Chemical Industries, Ltd. v. Alphapharm, Ltd.*, 492 F.3d 1350, 1362-63 (Fed Cir. 2007). Accordingly, it is urged that the obviousness rejection over Stern in view of Habener, Mandic or Barbier should be withdrawn.

Claims 5 and 48 stand rejected under 35 U.S.C. §103(a) as allegedly being obvious over the foregoing references as applied, and further in view Stern, U.S. Patent 5,912,014 ("Stern '014"). It is urged that Stern '014 does not overcome the deficiencies noted above in combining Habener, Mandic or Barbier with the teachings of Stern '918 to render obvious, *inter alia*, independent claims 1 and 45, from which claims 5 and 48 are dependent, respectively. Hence dependent claims 5 and 48 are believed to define non-obvious subject matter for the same reasons previously stated in connection with independent claims 1 and 45. Accordingly it is urged that the further rejection of claims 5 and 48 should be withdrawn.

Claims 1-3, 5-15, 17-37, 39-41, 43-46, 49-53, 55, 57-59 and 63 stand rejected under 35 U.S.C. §103(a) as allegedly being obvious over WO 02/043767 ("the '367 reference") in view of Habener, Mandic, or Barbier. However, the Examiner does not allege that the '767 reference discloses or suggests use of amidated peptides. Instead, the disclosure of amidated peptides is attributed to Habener, Mandic, or Barbier. However, as noted above in connection with the first obviousness rejection, Habener, Mandic, and Barbier also modify their peptides in a wide variety of other ways, and include un-amidated compounds. They prepare their molecular structures for different purposes than enhancing oral bioavailability as taught by Applicants. It is urged that one of skill in the art would not be motivated by the teachings of Habener, Mandic or Barbier to selectively choose amidated peptides to the exclusion of other peptides taught by Habener, Mandic or Barbier for insertion into the oral delivery system of the '767 reference. For this reason, it is urged that the foregoing obviousness rejection be withdrawn.

Claims 5 and 48 stand rejected under 35 U.S.C. §103(a) as allegedly being obvious over the'767 reference in view of Habener, Mandic, or Barbier as applied above , and further in view of Stern, U.S. Patent 5,912,014 ("Stern '014"). It is urged that Stern '014 does not overcome the deficiencies noted above in combining Habener, Mandic or Barbier with the teachings of the '767 reference to render obvious, *inter alia*, independent claims 1 and 45, from which claims 5 and 48 are dependent, respectively. Hence, dependent claims 5 and 48 are believed to define non-obvious subject matter for the same reasons previously stated in connection with independent claims 1 and 45. Accordingly it is urged that the further rejection of claims 5 and 48 should be withdrawn.

Claims 1, 5, 6, 17-19, 40 and 41 stand rejected 35 U.S.C. §102(a) as allegedly anticipated by Neugebauer. The Examiner alleges that the palmitoyloleoylphosphatidlyserine of Neugebauer is equivalent to Applicants' absorption enhancer. However, the palmitoyloleoylphosphatidlyserine of Neugebauer is used to study helix structure of various PTH truncates - - not to enhance oral delivery. Anticipation requires that every limitation of the claims be met. Here, however, Neugebauer does not disclose or suggest an "oral pharmaceutical composition" as recited in Applicants' claims. The Examiner is correct on page 8 of the office action, that a statement of "intended use" does not distinguish an otherwise anticipated product claim. However, Applicants' language "oral pharmaceutical composition" is not a statement of intended use. It is a structural limitation, a term understood in the industry to cover tablets, capsules and other oral dosage forms that are not discussed by Neugebauer. Accordingly, it is urged that the anticipation rejection should be withdrawn.

It is believed that the application is now in condition for allowance. Issuance of a notice of allowance is solicited.

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